REMARKS

Reconsideration of the present application in view of the above amendments and following remarks is requested respectfully.

Claims 25 and 27 to 32 are pending. Claim 25 has been amended. No claims have been added or canceled.

Applicants acknowledge and appreciate the withdrawal by the Examiner of the art rejection set forth in the Office Action dated June 18, 2003. The present Office Action includes rejections under Section 112 and for obviousness-type double patenting, which are discussed below.

Discussion of Rejections Under Section 112

The rejections under Section 112 are addressed in the order they appear in the Office Action.

The rejection based on the following statement, which appears in the Office Action, is respectfully traversed.

> The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims recite 'arylacetamide non-peptide kappa opioid receptor agonists,' which encompasses much larger scope than herein disclosed (pages 99-112 in the specification). The specification provide no written description with respect to the compounds other than those disclosed herein.

See Office Action, ¶4. Applicants respectfully disagree with this rejection, and submit respectfully that the subject matter defined in the claims as presented to the Patent Office in applicants' Reply dated May 7, 2002 is adequately described in the present application, in accordance with Section 112. Nevertheless, in an effort to facilitate prosecution of the present application, independent Claim 25 has been amended to recite that the defined non-peptide arylacetamide compounds are amine-containing, and that the compounds are substituted with at least one polar group. To the extent that the rejection under Section 112 is

maintained against the presently amended claims, applicants respectfully request that the Examiner consider the following remarks.

The descriptive portion of the application contains extensive teachings regarding the presently claimed arylacetamide compounds. In particular, the Examiner's attention is directed respectfully to the teachings in the application, for example, at page 8, line 1 to page 92, last line. In this section of the specification, applicants describe, generically and specifically, a wide variety of compounds that are representative of arylacetamide compounds as defined in the present claims. With regard to applicants' generic teachings, the present application states the following.

> Peripherally-acting κ agonists can be prepared by the attachment of polar groups to non-peptide κ opioid receptor selective agonists, such as the arylacetamides. In designing the peripherally-acting ligands, the introduction of the polar groups may result in either retention or enhancement of antinociceptive potency and selectivity and also may increase the polarity of the ligand sufficient to reduce or eliminate CNS penetration across the blood-brain barrier (BBB).

See application, p. 12, ll. 2-3. Immediately following the above text in the present application, applicants teach a prototypical arylacetamide compound which is described as containing an aromatic region, a central region, and an amine region, all of which may serve as suitable positions for attachment of polar groups to provide the present κ opioid agonists (page 12, lines 8 to 11).

Also included in the aforementioned section of the application is an extensive discussion of various exemplary classes of arylacetamide compounds within the scope of the present invention, identified as generic Formulas I, II, III and IV, and methods for synthesizing same. Working examples of exemplary species of the present arylacetamide compounds are also set forth. These exemplary classes of compounds, and exemplary species, are (1) kappa opiate receptor agonists which are (2) amine-containing, (3) non-peptide (4) arylacetamide compounds that are (5) substituted with at least one polar group. It is submitted respectfully that, in light of these extensive generic and specific teachings, as outlined above, the present application provides a complete written description of the subject matter defined in the present claims, as amended herein.

Claims 25 and 27 to 32 have also been rejected for containing subject matter not described in such a way as to enable one skilled in the art to make and use the claimed compounds. Applicants respectfully disagree with this rejection, and submit respectfully that the present application teaches how to make and use the full scope of the compounds defined in the claims as presented to the Patent Office in applicants' Reply dated May 7, 2002. However, as noted above, independent Claim 25 has been amended to recite that the defined non-peptide arylacetamide compounds are amine-containing, and that the compounds are substituted with .at least one polar group. To the extent that the rejections under Section 112 are maintained against the claims, as amended herein, applicants respectfully submit the following.

It is well-established that the first paragraph of Section 112 of the patent statute requires only objective enablement of the invention. How the teaching is set forth, either by the use of specific examples or broad terminology, is of no importance. *In re Marzocchi*, 169 USPQ 367 (C.C.P.A. 1971). Accordingly, when rejecting a claim under the enablement requirement, it is the PTO who bears the initial burden of setting forth technical reasoning as to why it is believed that the scope of protection is not adequately enabled. *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993). Without a reason to doubt the truth of the statements made in the patent application, the application must be considered enabling. *Id.*

Applying these tenets to the present situation, it is respectfully submitted that the present Office Action provides no such technical reasoning to support the opinion that applicants have not enabled the claimed compounds. In fact, the *only* reasoning provided in the Office Action for this conclusion is the unsupported assertion that "there are unlimited number of non-peptide compounds with an arylacetamide moiety". Mere statements, however, are insufficient to compel a conclusion of nonenablement. *In re Colianni*, 668 F.2d 1229 (C.C.P.A. 1982). The statements must be supported by objective evidence. *Id.*

Significantly, the Office Action concedes that the specification is enabling for species which are identified in Tables I-IV at pages 99 to 112 of the application. The Office Action contends, however, that the specification does not enable "other agents which may be termed arylacetamide non-peptide kappa opioid receptor agonists" because certain factors enumerated in *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988) call into question the degree to which the entire scope of the claims could be practiced. This contention apparently stems

from the subjective belief that the claims are too broad and more working examples are required.

Applicants respectfully submit that an application is not silent as to embodiments simply because they are not set forth as working examples. Such an interpretation misinterprets the present invention in an effort to limit its scope, and fails to consider the genus as a whole, as is required by law. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). What the present Office Action fails to appreciate is that for a claimed genus, representative examples, together with a statement applicable to the genus as a whole, will ordinarily be sufficient if one skilled in the art would expect the claimed genus could be used in the same manner without undue experimentation. M.P.E.P. 2164.02. The Office Action fails to provide any objective evidence as to why the "other agents" would not be expected to act in a similar manner as those exemplified.

It is also asserted that the amount of direction provided by the specification is insufficient. Applicants, however, have provided both generic and specific teachings, as well as one hundred and twenty-one working examples. The Office Action states that the specification is nevertheless lacking because "there are unlimited number of non-peptide compounds with an arylacetamide moiety" and that "[t]he specification or the claims provide no information or guidance as to the structural requirements that would make the arylacetamide to be a Kappa opioid receptor agonist." Applicants respectfully submit that this statement is erroneous in light of the teachings in the application, as discussed above, regarding exemplary peripherally-acting κ opioid receptor selective agonists which are amine-containing, non-peptide arylacetamides substituted with one or more polar groups. The four classes of exemplary arylacetamide compounds, identified as Formulas I, II, III and IV, together with the considerable number of working examples, provide numerous examples of such compounds, together with methods for their preparation. Biological testing procedures which may be used to readily evaluate the biological activity of the present arylacetamide compounds are set forth in the present application at page 93, line 24 to page 99, line 15, and at page 112, line 3 to page 113, line 14.

The Patent Office is essentially requiring that applicants teach how to make and use any and all compounds which are non-peptide arylacetamides, and which are kappa agonist compounds that are devoid of central nervous system effects. However, applicants are not

required, nor could they be reasonably expected, to meet this standard as it is higher than that imposed by law. Indeed, this subjective requirement places an undue burden on Applicants, frustrating the policy set forth by the Federal Circuit that "[i]t is crucial to provide researchers with an incentive to disclose pharmacological activities in as many compounds as possible." M.P.E.P. §2107.

Finally, the Office Action asserts that the amount of experimentation required to make and use the compounds defined in independent Claim 25 is undue. Applicants respectfully disagree. Compounds within the scope of Claim 25 can be assembled, for example, by the methods taught in the specification when taken in conjunction with methods well-known in the art, and it would require nothing more than routine experimentation to test functional equivalents of the working examples according to the methods, for example, described in the present application. Even assuming, *arguendo*, that some amount of experimentation may be involved in making and testing compounds other than those specifically exemplified does not, *a priori*, mean that the type and amount of experimentation is undue. *In re Angstadt*, 190 U.S.P.Q. 214 (C.C.P.A. 1986).

Because the Office Action fails to provide any objective evidence that it would take anything more than routine experimentation to make and use the compounds defined in Claim 25, and because such evidence is required to support the rejection under Section 112, first paragraph, applicants respectfully request reconsideration and the withdrawal thereof.

Discussion of Rejections for Obviousness-type Double Patenting

Claims 25 and 27 to 32 have been rejected for obviousness-type double patenting in view of claims in Zhang et al., U.S. Patent No. 6,239,154, Zhang et al., U.S. Patent No. 6,476,063, Zhang et al., U.S. Patent No. 6,486,165 and Zhang et al., U.S. Patent No. 6,492,351. The pending claims have also been provisionally rejected for obviousness-type double patenting in view of claims in copending applications Serial Nos. 10/455,687 and 10/455,545. To address these rejections, applicants submit herewith six Terminal Disclaimer documents and a Statement under 37 CFR 3.73(b). The Disclaimers are directed to disclaiming the portion of a patent granted on the present application that would extend beyond the terms of the patents cited in the obviousness-type double patenting rejections, and

the terms of any patents issued based on the applications cited in the provisional obviousness-type double patenting rejections.

In view of the enclosed Terminal Disclaimers, reconsideration and withdrawal of the rejections for obviousness-type double patenting rejections are requested respectfully.

Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record. Accordingly, an early and favorable reconsideration of the rejections and an allowance of all of pending Claims 25 and 27 to 32 are requested respectfully.

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